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Approaches Consideration in the Management of Hepatitis (Warm E Kabid) by Means of Conventional Medicines and Herbal Drugs: A Systematic Review Study

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Abstract

The word hepatitis comes from two words, the Greek word Hepar meaning 'Liver" and the Latin word itis meaning inflammation. Hepatitis refers to an inflammatory condition of the liver. It is commonly caused by viral infection, but there are other possible causes of hepatitis. These include autoimmune hepatitis that occurs as a secondary result of medications, toxicity, and alcohol. In Unani system of medicine hepatitis is a condition in there occur derailment in temperament of liver and due to this disturb temperament it may lead to increase in liver size and other symptoms. In Unani medicine hepatitis is treated by its holistic approach. The stalwarts' scholars such as Razi, Majoosi, Sheikh, Akbar Arzani, has classified the condition as sanguine, billious, phlegmatic and malencholic. Here in this paper an attempt is made to review the management of Hepatitis both in conventional therapy as well as by complementary and alternative (CAM) supplements usage.

Keywords: Hepatitis; Temperament; Complementary; Alternative (CAM)

Introduction

Hippocrates was the first Unani physician who described hepatitis with rational explanation based on humoural theories and human temperament. There was continuous pilling of knowledge by Galen and other Arab physicians, like Rbban tabri, Zakariya Razi, Majoosi, Maseehi, Jurjani, etc., and all they contributed a lot in its diagnosis and management. Hepatitis is a disease of liver that is characterized by the presence of inflammatory cells in the tissue of the organ. Hepatitis may occur without symptoms but can lead to jaundice as well. It can be manifest as either acute or chronic disease depending upon the cause [1]. Acute hepatitis can be self-limiting or may progress to chronic hepatitis and in this way can lead to acute liver failure in rare instances [2]. Chronic hepatitis may have symptoms or may progress to fibrosis and cirrhosis [3]. Cirrhosis of the liver can increase the risk of developing hepatocellular carcinoma [4].

Causes

Causes of hepatitis can be divided into the following major categories: infectious, metabolic, ischemic, autoimmune, genetic and other. Infectious agents include viruses, bacteria, and parasites. Toxins, drugs, alcohol, and lipids are metabolic causes of liver injury and inflammation. Autoimmune and genetic causes of hepatitis involve genetic predispositions and tend to affect characteristic populations. Ischemic hepatitis results from reduced blood flow to the liver as in shock, heart failure, or vascular insufficiency [5]. In infectious hepatitis three types of hepatitis comes into play, i.e., viral hepatitis, parasitic hepatitis, bacterial hepatitis.

Viral hepatitis

Viral hepatitis is the most common type of hepatitis and is caused by five different viruses' hepatitis A, B, C, D, E). Hepatitis A and E are transmitted by same feco-oral route and are self-limiting in nature and do not lead to chronic hepatitis on the other hand, hepatitis B, C and D are transmitted when blood and mucous membrane are exposed to infected blood and body fluids such as semen and vaginal secretions. Hepatitis B and C can present either acutely or chronically. Hepatitis D is a defective virus that requires hepatitis B to replicate and is only found with hepatitis B co-infection [1]. In adults, hepatitis B infection is most commonly self-limiting, with less than 5% progressing to chronic state, and 20 to 30% of those chronically infected developing cirrhosis and/or liver cancer [6]. Unlike hepatitis B, most cases of hepatitis C lead to chronic infection [7].

Etio-pathology of warm-e-kabid (Hepatitis) in Unani classical text

Rabban Tabri mentioned that warm-e-kabid muhaddab (swelling on the convex side of liver) occurs when kidney and diaphragm involved and when involvement of spleen, stomach, and intestines takes place it will be warm-e-kabid Maqar (swelling on the concave part of the liver).

Zakariya Razi mentioned that when liver absorbs useless substances due to su-e-mizaj har (abnormal hot temperament) than other necessary substances required by liver are unable to get absorb by liver and it will result in warm-e-kabid (hepatitis).

Ismail Jurjani mentioned that when due to a suddah (obstruction) between liver and gallbladder safra (bile) does not pass to duodenum it leads to accumulation of bile in liver and thus result in warm-e-kabid (hepatitis).

Abul Hasan Ahmad Bin Mohammad Tabri mentioned that when obstruction occurs between spleen and liver it leads to formation of improper blood and that accumulates in bile canaliculi and produces liver inflammation.

According to moalijat-e-nafisi and turjuma aqsarai any hot substance like safra muharriq (Burnt or oxidized bile) produces liver

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inflammation and results in hepatomagaly due to coverage of large area of the liver [8].

Causes as per classical Unani text

1. Sometimes hyperpyrexia and chronic fever predisposes hepatitis but sometime the inflammation is without fever and result in hepatomagaly. Excessive heat can result in hepatitis as well.
2. Many digestive disorders such as zoaf-e-meda (weak stomach) and constipation may be the cause of hepatitis as zoef-e-meda (weak stomach) in itself produces cold temperament which in turn a cause of warm-e-kabid (hepatitis).
3. Due to hyperactivity of stomach, the assimilating and absorbing power increases and because of this liver absorbs much matter which normally should not, this absorb matter causes inflammation of the liver.
4. Sometimes humours get accumulated in the liver because of emboli. If the obstruction is bilious and emboli are close to the gall bladder, the bile gets mixed with blood which irritates the vicinity of the liver and results in hepatomagaly. The excess of bile is one of the important causes of the liver inflammation [9].

Categorization of Hepatitis (warm-e-kabid) according to nature and sites of the warm in Greeko Arab medicines

1. Warm-e-kabid haar (abnormal hot temperamental hepatitis)/ warm-e-kabid falghamooni (cellulitic inflammatory hepatitis)- warm-e-kabid har (abnormal hot temperamental hepatitis)/ warm e kabid falghamooni (cellulitic inflammatory hepatitis) are caused by all those hot substances which create excess heat in the body. There occurs bilious vomiting, high fever, great thirst, hiccups, loss of appetite and nausea is present. All the above symptoms are occur when inflammation are found in the concavity of liver. There is pain which radiates to the back and neck. Hippocrates said that, indicative of warm-e-kabid haar are loose stool with some solid and some liquid parts with blackish color associated with heat. Crisis of warm-e-kabid haar begins with epistaxis, polyuria, excessive sweating, bilious diarrhea and vomiting. The special features of warm-e-kabid falghamooni are red face and more pronounced blood vessels.
2. Warm-e-kabid safrawi urooqi(vasicular and bilious hepatitis)- in this kind of hepatitis patient feels no heaviness but burning and irritation, tongue is blackish, urine is very dark colored. The color of the skin becomes yellowish and there is high paroxysmal fever. The symptoms are relieved by cold and moist things or drugs.
3. Warm-e-kabid barid (cold temperamental hepatitis) - there is feeling of heaviness at site of the liver. There is no fever or thirst but the tongue is blackish. There is some spasm in stomach. The patient's age, the previous treatment, diet, temperament and changes in the color of the body described before are the other symptoms which help in the diagnosis.
4. Warm-e-kabid sulb or sartani (hard or cancerous hepatitis)- usually it is result of some other inflammatory changes into a hard one and the hard enlargement is recognized by palpation. Patient feels pain and discomfort in the area of liver after taking food. This hard enlargement result in dropsy and is the first step towards cancerous. The blood plasma gets thick or solid and accumulates in the abdominal cavity and results in istisqa-e-ziqqi (water sac type ascites).
5. On the basis of four humors involved
   - Sanguinic liver inflammation
   - Billious liver inflammation
   - Phlegmatic liver inflammation
   - Melancholic liver inflammation
6. Avicenna classification in Al-Qanoon-Fit-Tib (canon of medicine)

1. Warm-e-kabid reehi (gaseous hepatitis)
2. Hard liver inflammation according to Avicenna there is two kind of hard hepatitis
   - Malignant hepatitis
   - Benign hepatitis
7. On the basis of its severity
   - Acute hepatitis
   - Chronic hepatitis
8. Zakariya razi classificationin Al-Havi-Fit-Tib (continens liber/ continence rasis, in English the virtue of life)
   - Obstructive hepatitis
   - Non obstructive hepatitis

Diagnosis and Test

1. ALT(Alanine aminotransferase) test
2. AST(Aspartate aminotransferase) test
3. Liver biopsy
4. Liver panel

What does the test result mean?

A low level of ALT in the blood is expected and is normal. Liver disease is the most common reason for higher than normal levels of ALT [10].

Very high levels of ALT (more than 10 times normal) are usually due to acute hepatitis, sometimes due to a viral infection. In acute hepatitis, ALT levels usually stay high for about 1-2 months but can take as long as 3-6 months to return to normal. Levels of ALT may also be markedly elevated (sometimes over 100 times normal) as a result of exposure to drugs or other substances that are toxic to the liver or in conditions that cause decreased blood flow (ischemia) to the liver.

ALT levels are usually not as high in chronic hepatitis, often less than 4 times normal. In this case, ALT levels often vary between normal and slightly increased, so the test may be ordered frequently to see if there is a pattern. Other causes of moderate increases in ALT include obstruction of bile ducts, cirrhosis (usually the result of chronic hepatitis or bile duct obstruction), heart damage, alcohol abuse, and with tumors in the liver. In most types of liver diseases, the ALT level is higher than AST and the AST/ALT ratio will be low (less than 1). There are a few exceptions; the AST/ALT ratio is usually greater than 1 in alcoholic hepatitis, cirrhosis, and with heart or muscle injury and may be greater than 1 for a day or two after onset of acute hepatitis.

ALT is more specific for the liver than is AST and is more commonly increased than is AST. Sometimes AST is compared directly to ALT and an AST/ALT ratio is calculated. This ratio may be used to distinguish between different causes of liver damage and to distinguish liver injury from damage to heart or muscle. AST may also be ordered, either by itself or with other tests, for people who are at an increased risk for liver disease since many people with mild liver damage will have no signs or symptoms. Some examples include:

- Persons who might have been expose to viral hepatitis
- Persons who are heavy drinkers
- Persons who have a history of liver disease in their family
- Persons taking drugs that can damage the liver
- Persons who are overweight and/or have diabetes [10]

When AST is used to monitor treatment of persons with liver disease, it may be ordered on a regular basis during the course of treatment to determine whether the therapy is effective. Normally, levels of AST in the blood are low. Very high levels of AST (more than 10 times normal) are usually due to acute hepatitis, sometimes due to a viral infection. With acute hepatitis, AST levels usually stay high for about 1-2 months but can take as long as 3-6 months to return to normal. Levels of AST may also be markedly elevated (often over 100 times normal) as a result of exposure to drugs or other substances that are toxic to the liver as well as in conditions that cause decreased blood flow (ischemia) to the liver. With chronic hepatitis, AST levels are usually not as high, often less than 4 times normal, and are more likely to be normal than are ALT levels. AST often varies between normal and slightly increased with chronic hepatitis, so the test may be ordered frequently to determine the pattern. Such moderate increases may also be seen in other diseases of the liver, especially when the bile ducts are blocked, or with cirrhosis or certain cancers of the liver. In most types of liver disease, the ALT level is higher than AST and the AST/ALT ratio will be low (less than 1). There are a few exceptions; the AST/ALT ratio is usually increased in alcoholic hepatitis, cirrhosis, and in the first day or two of acute hepatitis or injury from bile duct obstruction. With heart or muscle injury, AST is often much higher than ALT (often 3-5 times as high) and levels tend to stay higher than ALT for longer than with liver injury [10]. Liver panel also known as liver profile or liver function test. Liver panel test results are not diagnostic of a specific condition; they indicate that there may be a problem with the liver. In a person who does not have symptoms or identifiable risk factors, abnormal liver test results may indicate a temporary liver injury [11].

Hepatitis conventional management approach

First of all decides who needs treatment and what recommendations you have to follow in the best management of hepatitis. The guidance should cover the full spectrum of care from determining that needs treatment, to what medicines to use, and how to monitor people long term.

Key recommendations includes

1. First asses the stage of the liver disease to help identify who needs treatment by the use of simple non-invasive tests.
2. Prioritize treatment for cirrhosis patient – the most advanced stage of liver disease.
3. The use of two effective medicines for the treatment of chronic hepatitis, i.e., tenofovir 9-(2-Phosphonyl-methoxypropyly) adenine (PMPA), entecavir-2-amino-9-[(1S,3R,4S)-4-hydroxy-3-(hydroxymethyl)-2 methylidenecyclopentyl]-3H-purin-6-one and at last.
4. For the detection of liver cancer do regular monitoring using simple tests. These tests also predicts whether treatment is working, or if it can be stopped.
5. These two drugs (tenofovir, entecavir) have a very low risk of developing drug resistance, are easy to take as one pill once a day and have few side effects.

Approach Consideration

Acute hepatitis A- treatment for acute hepatitis A is necessarily supportive in nature. Hospitalization is done with patients whose nausea and vomiting places them at risk of dehydration [12]. Well no specific treatments exist for hepatitis A. your body will clear the virus on its own the liver heals within six months with no lasting damage.

Its treatment usually focuses on coping with signs and symptoms. You may need to: Rest, cope with nausea, Rest your liver [13].

Hepatitis B- acute hepatitis B does not need the treatment and as the case of hepatitis A because no well antiviral therapy is established. Supportive treatment recommendations are the same as for Hepatitis A. Lamivudine(1-[(2R,5S)-2-(hydroxymethyl)-1,3-oxathiolan-5-yl]-1,2-dihydropyrimidin-2-one), adefovir dipivoxil [2-(6-aminopurin-9-yl)ethoxymethyl-(2,2-dimethylpropanoyloxymethoxy)phosphoryl] oxymethyl 2,2-dimethylpropanoate, and other antiviral therapies appear to have a positive impact on the natural history of severe cases of acute HBV infection [14].

Synergistic approach for control of hepatitis B- for the best prognosis a synergistic approach is maintained to suppress viral load and to boost immune response by using immunotherapeutic interventions [15]. For the prevention of HCC(hepato-cellular carcinoma) by the inclusion of antiviral treatment like pagylated interferon (pegIFN α-2a) and nucleos(t)ide analogue is very much useful [16].Therapy is recommended for chronic active hepatits (abnormal level of aminotransfereses, positive HBV DNA, positive or negative HBeAg findings) [17,18].

NIH (national institute of health) recommendations for the use of nucleotide therapy

1. Acute liver failure
2. Cirrhotic patients (HBV DNA positive)
3. Those with clinical complications
4. Advanced fibrosis (HBV DNA positive)
5. Reactivation of chronic HBV during or after chemotherapy and immunosuppression.
6. In addition immunoglobulin should be administered to newborn born to women positive to HBsAg.

In general for HBeAg positive patients treatment is advised to those whose HBV DNA is above 20,000 IU/ml and ALT is elevated (ALT levels >20 U/L for females; 30 U/L for males) for 3-6 months [18].

For HBeAg-negative patients with chronic hepatitis B disease, treatment can be administered when the HBV DNA is at or above 2000 IU/mL (104 copies/mL) and the serum ALT is elevated (ALT levels >20 U/L for females; 30 U/L for males) for 3-6 months. In patients

co-infected with HBV and HIV, initiate therapy against HBV and administer antiretroviral therapy as well [19].

NIH (National Institute of Health) recommendations for not use of routine therapy who have the following

1. Chronic hepatitis B with high levels of serum HBV DNA but normal serum ALT levels or little activity on liver biopsy (immune-tolerant phase)
2. Low levels of or no detectable serum HBV DNA and normal serum ALT levels (inactive chronically infected/low replicative phase)
3. Positive serum HBV DNA but not HBsAg (latent HBV infection), unless the patient is undergoing immunosuppression.

Role of standard and pagylated interferon (pegIFN α-2a) and Lamivudine monotherapy in chronic hepatitis B

The main aim of treatment with lamivudine is to suppress the virus before there is irreversible damage in liver. Interferon alpha was the first line approved in most countries. This is beneficial in 30-40 percent patients but is expensive and has many unpleasant side effects. Interferon have antiviral, antiproliferative and immune-modulatory effects IFN alpha and IFN beta have predominantly antiviral effects but IFN gamma have more marked immunoregulatory but less potent antiviral activity [20]. A positive response to IFNa is usually defined as the loss of viral replication markers (HBeAg [in patients who were HBeAg-positive] and serum HBV DNA) at the end of treatment or 24 weeks after discontinuation of treatment. A decrease of serum HBV DNA usually occurs during treatment, but loss of HBeAg and seroconversion to HBe antibody (anti-HBe) may be delayed [21].

Adefovir dipivoxil

AdefovirDipivoxil[2-(6-aminopurin-9-yl)ethoxymethyl-(2,2-dimethylpropanoyloxymethoxy)phosphoryl]oxymethyl 2,2-dimethylpropanoate Tablets are indicated for the treatment of chronic hepatitis B in patients 12 years of age and older with evidence of active viral replication and either evidence of persistent elevations in serum aminotransferases (ALT or AST) or histologically active disease. This indication is based on histological, virological, biochemical and serological responses in adult patients with HBeAg+ and HBeAg- chronic hepatitis B with compensated liver function and with clinical evidence of lamivudine-resistant hepatitis B virus with either compensated or decompensated liver function. For patients 12 to less than 18 years of age, the indication is based on virological and biochemical responses in patients with HBeAg+ chronic hepatitis B virus infection with compensated liver function [22]. The recommended dose of Adefovir Dipivoxil Tablets in chronic hepatitis B patients for patients 12 years of age and older with adequate renal function is 10 mg, once daily, taken orally. Adefovir Dipivoxil Tablets is not recommended for use in children less than 12 years of age.

Hepatitis C

Patient with hepatitis c appear to have an excellent chance of responding with 6 months interferon standard therapy. It is useful because it has no definite timing of therapy and spontaneous chance of resolution, initiation can be recommended, however waiting 2-4 months after the onset of illness seems to be reasonable [23]. Initial treatment of HCV infection includes patients with chronic hepatitis C who have not been previously treated with IFN, PEG-IFN, ribavirin or any HCV direct-acting antiviral (DAA) agent. All patients should have careful monitoring during treatment, particularly for anaemia if ribavirin is included in the regimen. Specific recommendations are given when treatment differs for a particular group (e.g. those infected with various genotypes).

A. Genotype 1a patients without cirrhosis-Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) for 12 weeks is a Recommended regimen for treatment-naïve patients with HCV genotype 1a infection who do not have cirrhosis and in whom no baseline NS5A RAVs§ for elbasvir are detected [24].

B. Genotype 1a patients with compensated cirrhosis- Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) for 12 weeks is a recommended regimen for treatment-naïve patients with HCV genotype. 1a infection who have compensated cirrhosis and in whom no baseline NS5A RAVs§ for elbasvir are detected.

C. Genotype 1b patients without cirrhosis- Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) for 12 weeks is a recommended regimen for treatment-naïve patients with HCV genotype 1b infection who do not have cirrhosis

D. Genotype 1b patients with compensated cirrhosis - Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) for 12 weeks is a recommended regimen for treatment-naïve patients with HCV genotype 1b infection who have compensated cirrhosis [23].

Hepatitis D

The treatment for hepatitis D consists primarily of supportive measures. It is necessary to observe synthetic liver markers and mental status closely. Deterioration of either should prompt early consultation with hospital personnel capable of performing liver transplantation [24]. Liver transplantation is indicated in patients with fulminant liver failure. Patients with evidence of decompensated liver disease or fulminant liver failure should be immediately transferred to a center capable of performing a liver transplantation [25]. There has been no approval of pharmacologic treatment in hepatitis D virus. However a study of efficacy of peginterferon alpha 2a (pegIFN a2a) found that treatment with or without adefovir resulted in sustained HDV RNA virus clearance in approximately one fourth of patients [25,26]. No vaccine available for HDV but the hepatitis B vaccination is sufficient.

Hepatitis E

Management should be predominantly preventive based on clean drinking water, personal hygiene, and good sanitation [27]. It is preventable by vaccination. A study in Nepal and china had shown the efficacy of recombinant genotype 1HEV vaccine in preventing infection and clinical disease [28,29]. This vaccine not only prevents the genotype1 HEV, genotype 4 HEV also prevented. Vaccine efficacy for genotype 3 is not known [30].

Treatment of Acute hepatitis E infection- It only requires symptomatic treatment in immunocompetent persons, as almost all of them are able to clear the virus spontaneously. A report has shown significant improvement after treatment with ribavirin for 21 days [31]. Although ribavirin therapy is contraindicated in pregnancy owing to teratogenecity the risks of untreated HEV to the mother and fetus are high and tials of antiviral therapy might be worthwhile [32].

Treatment of chronic hepatitis E infection- In transplant recipients with chronic HEV viral clearance is desirable. First of all reduction

in immunosuppressive therapy in immunocompetent clears the virus in approximately 30% of patients mycophenolic acid (including prodrug mycophenolate mofetil) inhibits the HEV replication in vitro. Steroids were found not to influence HEV replication *in vitro* [33-35]. Although data are limited, ribavirin monotherapy (600–1000 mg/day) for at least 3 months seems to be the first treatment option for patients with chronic hepatitis E who are not able to clear HEV after immunosuppression is reduced [36]. However, the presence of G1634 mutation in the RdRp domain of HEV ORF1 protein was reported to be associated with ribavirin treatment failure. In this situation, pegylated interferon alfa may be used as an alternative treatment option if there is no contraindication [37]. Treatment with pegylated interferon alfa for 3-12 months has led to sustained clearance of HEV RNA in patients with chronic hepatitis E who underwent liver transplantations [38,39]. However, interferon therapy can cause significant adverse effects and organ rejection in transplant recipients, especially those who have undergone heart or kidney transplantation.

Unani medicinal approach - In Unani system of medicine a large number of single and poly herbal preparations have been documented in the treatment of hepatitis. These preparations have been proved for their efficacy in chronic

Hepatitis B so it is now important to do more research to validate and revalidate the efficacy of these preparations mentioned in Unani literature along with the mechanism involved in the antiviral action of the herbal medicines. Some of these poly herbal formulations act by purifying the morbid material from the body. In this regard a study by Mohammad Akhtar Siddiqui and Shabnam Ansari has been done in department of moalijat, Majeedia hospital Jamia Hamdard, New Delhi, to show the efficacy of Unani formulation on viral load in chronic hepatitis B. the study shows that Unani formulation in the form of decoction of six plants, viz. shahtara (*Fumaria officinalis*), sarphookah (*Tephrosia purpurea*), chiraita (*Swertia chiraita*), gule mundi (*Sphaeranthus indicus*) and sandal surkh (*Pterocarpus Santalinus*) harboures in complete relief in symptoms such as loss of appetite, jaundice, fever, general weakness, pain in abdomen, flatulence after one and two weeks treatment. The treatment was carried for 6 months to evaluate its effect on serum HBV DNA quantitative value. The study shows that HBV DNA became undetectable at an average of 14 weeks of treatment. The ideal aim of any therapy is to eradicate the HBV DNA and HBsAg and the virus from the body. Nevertheless, HBV DNA quantitative value is marker of viral infectivity and its replication. Nevertheless, HBV DNA quantitative value is marker of viral infectivity and its replication. A higher quantitative HBV DNA which prolongs for long period increases likely chances of developing hepatocellular carcinoma. So treatment with Unani formulation in these cases eradicated HBV DNA which showed the ability of the formulation to suppress the virus replication and removing the risk for developing end stage liver diseases. Treatment with nucleoside analogue in CHB such as tenofovir which produces undetectable HBV DNA in 95% of the patient after one year (48 weeks) of therapy while with our formulation undetectable HBV DNA occurred more rapidly (maximum 23 weeks) along with improvement in their symptoms. The suppressive effect on these viral markers possibly could be due to constituents of the preparation, which have been proved for their potential antiviral, immunomodulator, hepatoprotective, anti-inflammatory and antioxidant activity in various animal models [40]. Another more therapy, i.e., venesaction which comes under regimental therapy along with oral medications is useful in hepatitis The study has been done in the same aforesaid department of same institute in Jamia Hamdard University New Delhi by Fasihuzzaman et al. entitled as "Chronic hepatitis B treated with oral Unani medications along with FASD (venesaction)

The study shows that the use of Unani medications such as Sharbat Jigreen (syrup jigreen) which is mukawi jigar (hepatoprotective) used in the present study. Capsule Jigreena has main constituent as Revind cheeni (Rheum emodi) which has known hepatoprotective and antioxidant activity. Jawarish pudina walaiti (semi solid preparation) and Jawarish anarain are appetizers thus help in proper digestion. Sharbat dinar was given for proper bowel movements. Sharbat bazoori (syrup bazoori) was given for decreasing the bilirubin levels. Its strong diuretic effects it increases the excretion of urobilinogen from the body and also has known anti-inflammatory action. Habbe-kabid naushadri (pills) and Arq makooh (distilled water in the form of vapours) increase the appetite and decrease the flatulence. Arq makooh is known hepato-protective drug and has anti-inflammatory effect on liver.

Dose of the oral treatment- Oral treatment included Sharbat Jigreen 20 ml BD, Capsule Jigreena 2 BD, Arq Makooh 50 ml BD, Majoon Dabidul Warad (drugs powder mixed with honey or sugar solution) 10 g BD, Sharbat Bazoori (syrup bazoori) 25 ml BD, Jawarish Pudina Walaiti 10 g evening, Jawarish anarain 10 g after meals, Hab-e-Kabid Naushadri (pills) 1 TDS. The treatment was given for 4 months. Fasd (venesection) was done thrice in the study consecutive for three months under aseptic conditions.

Recovery after treatment - A spontaneous recovery of patient was noted initially with improvement of sign and symptoms. Then it was noted that bilirubin levels came down frequently along with SGOT and SGPT followed by HbsAg became negative showing virus is not replicating in the body. HBV-DNA analysis was done and significantly showed decrease levels after one month and finally became more then detectible [41].

Use of herbal supplements and other complementary approaches in hepatitis

Silymarin (milk thistle) - Silymarin from the milk thistle herb (*Silybum marianum*) is used by many patients with chronic viral hepatitis, but its efficacy remains unknown. Silymarin treatment results in a decrease in serum transaminases [42]. There is no evidence that silymarin affects viral load or improves liver histology in hepatitis B or C. no study shows that, the use of silymarin concomitantly with interferon, nucleoside analogues, or other conventional treatments for hepatitis B or C. In conclusion, silymarin compounds likely decrease serum transaminases in patients with chronic viral hepatitis, but do not appear to affect viral load or liver histology. Nevertheless it may be worthwhile to determine its effects in conjunction with standard antiviral treatment. Silymarin is a mixture of biologically active substances extracted from milk thistle seeds. A March 2013 "Hepatology" review of published studies on silymarin reports that this herb has consistently demonstrated anti-inflammatory and antioxidant effects in a laboratory setting [43].

Humoral dynamic of milk thistle-Sanguine-cleanses the blood Phlegmatic - a mild expectorant that has demulcent and emollient properties to soften and liquefy phlegm, as well as mildly astringent properties to aid in the expulsion of phlegm; also a mild diuretic. Choleric - a choleretic/cholagogue that improves the generation and secretion of Yellow Bile. Melancholic - one of the best remedies for aggravated Black Bile known.

Cautions and contraindications

Milk Thistle is not only very balanced and temperate in its overall

nature and temperament, but it is also very mild and nontoxic; in fact, its chief virtue is to help the liver detoxify itself from noxious poisons and toxins. Caution and monitoring may be necessary when taking Milk Thistle if you are taking prescription anti-diabetic drugs, as Milk Thistle has a mild lowering effect on blood sugar, and may enhance or increase the effectiveness of these drugs. And so, adding Milk Thistle as a supplement may require a readjustment of the dosage of prescription anti-diabetic drugs. The addition of Milk Thistle can also be effective in protecting the liver from damage caused by many prescription medications, including anti-diabetic and cholesterol lowering drugs [44].

Medicinal uses

As a hepatoprotector to help the liver detoxify from food, metabolic, chemical and environmental toxins. To remove obstructions from the liver and spleen in jaundice, hypochondriac fullness and distension and melancholia. To help heal the liver and regenerate liver cells in hepatitis, cirrhosis and fatty liver disorders. As a galactogogue to improve the flow of breast milk in nursing mothers. As an anti-diabetic and hypolipidemic dietary supplement to help lower high blood sugar and cholesterol. A tea made from the leaves is very effective as a stomachic and carminative in an agitated or upset stomach [45].

Preparation and dosage

The most common form in which Milk Thistle is taken is as the concentrated extract of the seeds, which is called Silymarin. This is commonly available in pill or capsule form in health food stores, in which the usual dose is from one to two capsules, containing from 150 to 300 mg. of the extract, once or twice per day. Any dosage beyond this must be handled with caution and respect; although the extract in itself is very mild and nontoxic in nature, large doses may provoke strong cleansing and detoxification reactions in the liver and in the rest of the body as a result. The leaves of Milk Thistle can be brewed up as a tea, with one heaping teaspoon per cup of water for beverage purposes, and one heaping tablespoon per cup for medicinal or therapeutic purposes [45].

Classic combinations

With Chicory root to cleanse and detoxify the liver. With Fenugreek seed to stimulate milk production in nursing mothers and to stimulate liver metabolism and function. With Juniper berries to stimulate liver and digestive function. The leaves of Milk Thistle can be combined with Sage as a soothing and healing stomachic, and to improve liver and stomach function [45].

Licorice

Licorice, which contains a chemical glycyrrhizin, is found to have some beneficial effects in the treatment for hepatitis C. This supplement has shown to prevent the occurrence of liver cancer in chronic hepatitis C patients [44].

Other natural supplements including thymus extract, ginseng, schisandra and sophora roots are also used in hepatitis C treatment. However, laboratory studies have not proven the health benefits of these supplements. The natural supplements that should be avoided are kava, vitamin A, beta carotene and iron, since they can get deposited in the liver and cause complications. High doses of essential fatty acids can cause fatty liver and should be avoided. Some of these natural supplements contain contaminants like arsenic, cadmium, mercury, thallium, and lead. These are all toxic substances that can cause harm to the body.

Role of syrup kabdeen and liver-52 in hepatitis

Constituents of syrup kabdeen- Balchar (*Valeriana jatamasi*), Branjasif (*Achillia mallifolium*), Bekh kasni (*Cichorium intybus*), Tukhm e bathua (*Chenopodium album*), Tukhm e khayaren (*Cucumis sativus*), Tukhm e kasni (*Cichorium intybus*), Tukhm e kasoos (*Cuscutta reflexa*), Chiraita shireen (Swertia chirata), Khoolanjan (*Alpinia galanga*), Revand chini (*Rheum emodi wall*), Shahtera (*Fumeria officinallis*), Satar farsi (*Zataria multiflora*), Ushba maghribi (*Smilex aspera*), Uood e hindi (*Aquillaria agalocha*), Kasaundi (*Cassia occidentalis*), Gul e tisu (*Butea frondosa*), Gul e surkh (*Rosa domestica*), Gule ghafis (*Agrimonia eupatorium*), Gul e nilofer (*Nymphea alba*), Mako khushk (*Solanum nigrum*), Narmushk (*Mesua farea*), Qand safed (cane sugar) [8].

Constituents of Liv-52

Himsra (*Capparis spinosa*), Kasni (*Cichorium intybus*), Mandura Bhasama (*Farric oxide calx*), Kakamachi (Solanum nigrum), Arjuna (*Terminalia arjuna*), Kasamada (*Cassia occidentalis*), Brinjasipha (*Achillia millifolium*), Jhavuka (*Tamarix gallica*) [46].

A study which has been done in Ajmal Khan Tibbya College Amu Aligarh. On the role of syrup kabdeen, liver-52 and lamivudine in patients with hepatitis, the study shows that, after receiving kabdeen and liver-52 jaundice disappeared after 45 days of treatment. Patients who received lamivudine jaundice disappeared after 1 month due to its inhibiting HBV replication and reverse transcriptase activity. In kabdeen group the improvement may be due to the presence of kasni, mako, Gul-e-tesu, Revand chini, sumbuluteeb, Tukhm-e-bathua and od-e-hindi, which is useful clearing the excess bile pigments from blood. The slightly better improvement in Liv-52 group may be due to additional action of kibr, arjuna, mykalan, which has diuretic, anti-inflammatory, and hepatotonic actions. Overall improvement in hepatomagaly was maximum for, i.e., 85.71% in lamivudine group, followed by 75% in Liv-52 and 71.42% in kabdeen group as per the study done.

Discussion and Conclusion

As we know liver plays a very careful role in the catabolic and anabolic activities of the human body. It performs a wide variety of functions like metabolism, protein synthesis, coagulation functions and excretion of bile, and hormones. Due to its dual supply of blood from hepatic artery and portal vein it is affected in several ways invariably. Like any other organs it is also exposed to infective agents who may reach it either through hepatic artery in systematic infections or by portal vein gastrointestinal infections. Probably the most common infection affecting the liver is of viral etiology. The aim of this review is to summarize different conventional, herbal and supplementary approaches used in the management of chronic hepatitis infection and focusing on both the class main effects differently. All nucleoside analogs have a "Black Box" warning because of their potential for inhibition of human DNA polymerase gamma involved in mitochondrial DNA replication. A reduction in intracellular mitochondrial DNA levels can lead to varying clinical manifestations of mitochondrial toxicity (i.e., neuropathy, myopathy, lactic acidosis). There are some other dose dependent side effects of antiviral therapies like adefovir and tenofovir, etc. There are several viruses causing hepatitis with symptoms ranging from mild to severe. Conventional medicinal treatments are available for hepatitis c and viruses; however, some people also try complementary and alternative medicine (CAM) therapies, especially herbal supplements. As per from the above mentioned studies which has been done to prove the efficacy of herbal formulations in minimising or mitigate symptoms having less or none side effects which usually perceived by long term

conventional antiviral treatment. However it is important not to replace conventional medicinal treatment with that of complementary and alternative therapies. Complementary therapies what is mentioned above do something better in managing your health. NCCAM supported research shows silymarin effectiveness for preventing and reversing the complications of chronic hepatitis C and in people who did not respond to conventional antiviral treatment and in whom with non alchohalic steatohepatitis. People with chronic liver disease sometimes use licorice root or its extract glycyrrhizin. Some studies, reported from outside the United States, have looked at glycyrrhizin administered intravenously for hepatitis C. Preliminary evidence from these studies suggests that glycyrrhizin may have beneficial effects against hepatitis C. However, additional research is needed before reaching any conclusions. So lastly, this is to declare that, from the above mentioned studies which has been done in the department of medicine in Jamia Hamdard and Ajmal Khan Tibyya Collage using sharbat jigreen (syrup jigreen) and sharbat kabdeen (syrup kabdeen) shows the improvement in symptoms due to hepatitis with their ingredient properties of having hepatoprotective, immunomodulators, anti-inflammatory, diuretic and clearing the excess bile from blood without imposing side effects as found in conventional therapies but this is strongly recommended not to replace proven conventional treatments with CAM treatments that are unproven at some researches.

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